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EXAMINER	
LEAVITT, MARIA GOMEZ	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,098	GOLETZ ET AL.	
	Examiner	Art Unit	
	MARIA LEAVITT	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,7,9-12,20 and 22-24* is/are pending in the application.

4a) Of the above claim(s) *7,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,11,12,20 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04-27-2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 1, 3, 5-7, 9-12, 20, 22-24 are pending. Claims 1 and 3 have been amended, and claims 23 and 24 have been added by Applicant's amendment filed on 04-27-2009. Claims 7, 9 and 10 were previously withdrawn from consideration as being directed to non-elected invention pursuant to 37 CFR1.14(b), there being no allowable generic or linking claim. In response to the species election, applicant's election with traverse of lymphoma as the type of cancer was previously acknowledged.
3. Accordingly, claims 1, 3, 5, 6, 11-12, 20, 22-24 are currently under examination to which the following grounds of rejection are applicable.

Withdrawn Objections/Rejections in response to Applicants' arguments or amendments

Information Disclosure Statement

The following references have been considered by the examiner, as indicated on Form PTO 892: Ichiyama (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110) and Goletz (2003, *Adv Exp Med Bio*, pp. 147-62; p. 156).

Claim Objection

In view of applicants' amendment of claims 1 to spell out the abbreviations TF and MUC1, objection to claims 1, 11 and 20 has been withdrawn.

Claim Rejections - 35 USC § 112-Enablement

In view of applicants' filing of a Deposit Declaration on 04-27-2009, rejection to claim 3 subparts (a) and (b) under 35 U.S.C. 112, first paragraph, specifically stating that cell lines i.e., NM-F9 accession number DSM ACC2606 and cell line NM-D4 accession number DSM ACC2605 have been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122, has been withdrawn.

In view of the withdrawn rejection, applicant's arguments are rendered moot.

Rejections/objections maintained in response to Applicants' arguments or amendments

Claim Rejections - 35 USC § 112-Enablement

Claims 20 and 22 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The specification does not provide enablement for claims directed to methods of treating or preventing lymphoma in a subject by administering a cell line expressing TF, MUC1 and glycophorin on its surface as broadly claimed. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

Response to Applicants' Arguments as they apply to rejection of Claims 20 and 22 under 35 U.S.C. 112, first paragraph

Applicants' arguments at pages 8 to 19 of the Remarks filed on 04-27-2009 have been fully considered but they are not persuasive. Applicants essentially argue that: 1) the examiner

merely generalizes that different lymphomas required different therapeutics and empirical testing is needed to apply any particular therapeutic to each type of lymphoma, as such testing constitute undue experimentation, 2) the rejection do not address how cells expressing TF, MUC1 and glycophorin, can be used to raised immune responses *in vitro* and *in vivo* in a model for the human immune system, 3) the skilled artisan would believe that Applicants' result reasonably correlate with the claimed methods of treating lymphoma because the art recognizes that these antigens are expressed on a wide array of cancers, immunotherapy is accepted approach for treating cancer, and sufficient disclosure has been provided showing *in vivo* that lysates of the claimed cell products successful induce an immune response of all three MUC1, TF and glycophorin G in a model of the human immune system, 4) a person of ordinary skill in the art needs to only follows the teaching in the application to test a particular cancer by using cells expressing MUC1, TF, and glycophorin on the surface in an amount effective to treat a disorder by eliciting an immune response, 5) the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled, 6) Goletz supports the enablement of Applicants claims by disclosing that TF antigen, in addition to being an excellent marker for tumors, may play a role in metastasis in the liver and endothelium and the fact that Goletz contemplates the promising role of TF antigen in cancer immunotherapy based on the early success by others in treating advanced cancer with enzymatically desialylated glycophorin which carries high densities of TF.

Regarding 1), it is unclear how empirically testing of prospective embodiment, as well as future embodiments as the art progresses, that would be required to practice the invention as it is

claimed in its current scope, do not constitute undue experimentation. Applicants' opinion is not supported by any evidence.

Regarding 2) and 3), the Examiner notes that Applicants are trying to equate the induction of an immune response with an effective treatment of lymphoma (e.g., elected cancer species). In contrast to applicant arguments, the presence of antibodies against MUC1, TF and AGPA and induction of T helper immune responses does not imply an immune protective response, as the simply binding of the antibody molecules raised against microbial MUC1, TF and AGPA epitopes on surface of tumors does not necessary suppress or prevent incidence of tumor cells. As clearly disclosed in the publications of Clayman, Dictionary of Immunology, Fundamental of Immunology, Leffell, Luftig and others, submitted by Applicants, as part of the IDS of 04-27-2009, the immune system and responses are complexed and essentially divided into an innate immune system, and acquired or adaptive immune system in vertebrates, each of which contains humoral and cellular components. Though Applicants ccontemplate that NM-F9, for example, could be administered directly to a subject and, because of the hypersensitivity of NM-F9 to NK cells, NM-F9 would be lysed by NK cells leading to exposure of dendritic cells (DC) to necrotic lysates of transformed NM-F9 resulting in maturation of DC and induction of naive cytotoxic T cells against MUC1 and AGPA expressed in functional mature dendritic cells as well as expressed in lymphoma cells, it is unclear how the contemplated activation of naive cytotoxic T cells against MUC1 and AGPA would constitute and effective immune response against lymphoma. As stated in the previous office action, humans develop many types of lymphomas of different etiology, e.g., mucosa-associated lymphoid tissue, B-cell lymphoma, T cell lymphoma, gastric lymphoma and the specification fails to provide guidance as to which

type of lymphoma would be suitable for treatment by administration of NM-F9 as contemplated. Moreover, the specification as filed fails to provide particular guidance to resolve the known unpredictability in the art associated with treatment of lymphoma in a subject which included *de novo* determination of effective target sites, modes of delivery, safe administration of at least transformed NM-F9 cells to by lysed by NK cells so as to lead to maturation of DC and induction of naive cytotoxic T cells against MUC1 and AGPA to appropriately target lymphoma cells, requirement for repetitive treatment, level of expression required, cell number and others, and further, whereby treatment effects are provided for the claimed lymphoma condition. Applicants have not addressed the foregoing issues which go beyond merely raising an immune response in a subject and have to be enabling regarding the patentability of the invention.

Regarding 4) and 5), as stated in the previous office action, the specification does not disclose any examples of an *ex vivo* method of treating a subject with a condition characterized by a lymphoma. Though an enabling disclosure does not required working examples, the instant claims have been examined in accordance with the *Wands* factors and the teachings of the specification **as a whole**. The *Wands* factors include the presence or absence of working examples and to the extent the instant rejections are not sufficiently supported by an enabling disclosure in combination the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims, the disclosure is not enabling for the breadth of the claims. Applicants have not provided any evidence as to what type of lymphomas would be suitable for treatment or prevention in the method as claimed. Additionally, as stated in the previous action, there are currently many difficulties in creating correlatable animal models for cancer therapy because of its high level of

unpredictability in the art as evidenced by the disclosure of Carbon (Seminars in Cancer Biology, 2004, 14: 399-405) highlighting the unpredictability of the past 40 yeast treating any type of tumor cancer. The skilled artisan would have to determine how the induction of MUC1 and AGPA antibodies and cytotoxic T could effectively treat or prevent cancer as the specification is inadequate in describing and enabling the treatment and prevention of any type of lymphoma.

Regarding 6), there is not evidence that treatment of advanced breast cancer by administration of crude preparation of enzymatically desialylated glycophorin form O RBC carrying high densities of TF in a formulation with *Salmonella* type vaccine administered intradermally every 6-20 weeks after surgery is predictive of the success of treating lymphoma in the methods as claimed as breast cancer and lymphoma differ in etiologies and therapeutic end points. It is acknowledged that the present working examples demonstrate *in vivo* induction of an IgG and IgM antibody responses in NOD/SCID mice reconstituted with human PBMC that were vaccinated with NM-F9 cell lysates. However, beyond this affect there is no evidence that delivery of NM-F9, NM-D4 alone or combinations thereof, would treat or prevent any type of mucosa-associated lymphoid tissue, B-cell lymphoma, T cell lymphoma, gastric lymphoma and other lymphomas.

Claim Rejections - 35 USC § 102

Claim 1 remains rejected under 35 U.S.C. §102(b) as being anticipated by Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of record) as evidenced by Benoist et al., (1992, Immunology Letters, pp. 45-55) and Karsten et al., (1998, Cancer Research pp. 2541-2549, of record)

Response to Applicants' Arguments as they apply to rejection of Claim 1 under 35 USC § 102

At pages 19 and 20 of remarks, Applicants essentially argue that the present application shows that, 1) K562 cells do not express TF antigen (Fig. 1, pages 6-7, 10) and allege that the specification clearly discloses selecting for strong and stable expression of the tumor-specific TF antigens, a property that parental K562 did not possess, 2) Karsten only discloses synthetic peptides derived from MUC1 and engineered to contains TF elicited enhanced binding of some MUC1 antibodies and does not teach that the full length MUC1 containing TF is transformed into the K562-derived cells of Ichiyama, 3) Applicants have evidence that MUC1 from untreated K562 cells was shown to be TF negative and can only exhibit any TF after neuramidase treatment. Applicants conclude, "Karsten does not teach (or suggest) that the MUCl-transformed cells described in Ichiyama express the TF antigen and Applicants have provided strong evidence to the contrary". Applicants' arguments have been fully considered but they are not persuasive.

Regarding 1) and 3), the ability of mutagenized K562 cells to strongly and stably express the core glycotope TF is not disputed. However, lack of detection of TF in a binding assay is not evidence that the TF antigen (glycotope) (Galβ1-3GalNAcα-O-Ser/Thr (Core 1)) does not exist in the MUCl-transformed K562 cells of Ichiyama which are transfected with the full length MUC1 molecule. Conceivable, expression level of TF in GPA (specification page 6, lines 5-15) may be below the threshold limit for immune detection or the TF antigen may not be sufficiently exposed to be recognized by specific binding antibodies. The fact that enzymatic desialylation with neuramidase treatment leads to strong and stable expression of the core glycotope TF,

appears to suggest that TF was present in K562, however, access to the TF glycotope in MUC1 and/or glycophorin was inhibited by the presence of terminal sialic acids in the MUC1 and/or glycophorin. How could the strong and stably expression of TF in NM-F9 and NM-D4 explained if the glycotope was absent in parental K562?.

Regarding 2), the generation of synthetic peptides derived from MUC1 and engineered to contain TF is not disputed. However, Karsten suggest the presence of TF in the tandem repeat comprising the DTR motif (see for example, page 2545, col. 2; p. 2549, col. 1). To the extent that the breadth of claim 1 encompasses any cell line which expressed on the cell surface TF, MUC1 and glycophorin, including TF-MUC1, the disclosure of Ichiyama M, as evidenced by Benoist et al., and Karsten et al., anticipates the instant invention.

Claim Rejections - 35 USC § 103

Claims 1, 5, 6, 11 and 12 remain and **claim 24** is newly rejected under 35 USC 103 as being unpatentable over Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of record) as evidenced by Hinoda (2005, Journal of Clinical Laboratory Analysis, pages 100 – 104, Abstract), in view of Benoist et al., (Immunology Letters 1992, pp. 45-55) and Karsten et al., (1998, Cancer Research pp. 2541-2549, of record) and further in view of Horton et al., (U.S. Patent 7,268,120, Date of filing Apr. 21 2000).

The combined teachings of Ichiyama Benoist et al., Karsten et al and Horton et al are set forth at pages 13 and 14 of the previous Office action of 01-27-2009.

In addition, Ichiyama discloses detection of MUC1 with the monoclonal antibody (MAb) MUSE11 which recognizes the continuous amino acid sequence PDTRPAPG as evidenced by

Hinoda. The examiner believes this is the same sequence recognized by the TA-specific antibody and identified in the specification as filed at page 7, lies 5-10, as tumor-associated MUC1 epitope i.e. TA-MUC1. The TA-MUC1 is commonly known in the art and dffers from normal MUC1 by modified glycan side chains, absent evidence to the contrary.

Response to Applicants' Arguments as they apply to rejection of Claims 1, 5, 6, 11, 12 and 24 under 35 USC 103

At page 22 of remarks, Applicants essentially argue that: 1) the present application demonstrates that K562 cells do not express TF antigen as evidenced in Fig. 1, 2) transforming K562 cells with a plasmid encoding MUC1, as described in Ichiyama, does not change this fact, since, unlike the synthetic MUCl-derived glycopeptides engineered to contain TF described in Karsten, MUC1 expressed by K562 cells does not contain TF, 3) the '120 patent contains no teachings or suggestion that transformation of a cell with any nucleic acid would lead to TF expression, 4) even if the cited references did offer some teaching or suggestion to make the claimed cells--and Applicants submit that they do not--Applicants have shown that the claimed cells exhibit unexpected and beneficial properties, which would rebut a prima facie obviousness rejection. Applicants' arguments have been fully considered but they are not persuasive.

Regarding 1) and 2), as set forth in the paragraph above, the ability of mutagenized K562 cells to strongly and stably express the core glycotope TF is not disputed. However, lack of detection of TF in a binding assay is not evidence that the TF antigen (Galβ1-3GalNAcα-O-Ser/Thr (Core 1)) does not exist in the MUCl-transformed K562 cells of Ichiyama which are transfected with the full length MUC1 molecule. Conceivable, expression level of TF in GPA (specification page 6, lines 5-15) may be below the threshold limit for immune detection with an

immunofluorescence microscope or the TF may not be accessible for binding by the antibody. Karsten complements the teachings of Ichiyama M by disclosing that K562 cells transformed with the MUC1cDNA encoding for the full length tumor-associated epithelial human mucin. MUC1 implicitly comprise TF in the tandem repeat comprising the DTR motif (see for example, page 2545, col. 2; p. 2549, col. 1).

Regarding 3) note that the instant claims are product claims. All what is required in the claimed invention is the structure recited in the claim. Applicants have not provided an example of a structural limitation that was not address. All what is required by claim 1, for example, is a cell line comprising on the cell surface TF, MUC1 and glycophorin. Applicants have not provided evidence that MUC1 does not does not comprise the mucin-type O-glycan core 1, TF. There is no reason to believe that the properties of the claimed cell population would differ from the combined disclosure of Ichiyama, Karsten, Benoist and Horton based on being K562 cell lines contransfected with tumor-associated epithelial human mucin MUC1cDNA, implicitly expressing TF, and glycophorin on the cell surface. Insofar as Applicants' assertion of unexpected results and beneficial properties, it is noted that "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)" [MPEP 2112 under the heading "Requirements of Rejection Based on Inherency; Burden of Proof"] .

New grounds of objection/ rejection

Claim Objection

Claim 24 is objected to because of the following informalities: abbreviations such as TA-MUC1 should be spelled out at the first encounter in the claims. Appropriate correction is required.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 04-27-2009 is not in compliance with the provisions of 37 CFR 1.97.

The following references: Fundamental Immunology (Paul, Raven Press, NY), Leffell Mary (Human Immunology Handbook, pp. 1-45) and Snippe et al., (Vaccine Design) are incomplete in the absence of a publication date. The references are considered but they are lined-through the IDS citation because it did not contain the date, so it will not be published.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- First paragraph- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 subpart (c) is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by amendment of the claims in the response filed on 04-27-2009.**

Claim 3, subpart (c) recites "subclones of (a) or (b) which express on the cell surface TF, MUC1 and glycophorin". Thus claim 3, subpart (c) is broadly drawn to a genus of subclones derived from NM-F9 (Accession number DSM ACC2606) and NM-D4 (accession number DSM ACC2605) and required to express surface markers TF, MUC1 and glycophorin (GFP) in any undisclosed density with undefined modifications, e.g., the subclones may be conjugated to other cells, coupled to other proteins/peptides, cell surface makers may be stably or transiently expressed, GFP and MUC1 may be TF-GFP positive and/or TF-GFP negative, cells may be chemically modified.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

The specification as filed discloses the generation of NM-F9 and NM-D4 from K562 cells (ATCC CCL-243) by mutagenesis for stable TF expression, and NM-D4 cells were then selected from NM-F9 cells after further treatment for MUC1 expression. However, the specification is silent about any other selection process to generate clones from NM-F9 (Accession number DSM ACC2606) and NM-D4 (accession number DSM ACC2605). This disclosure is not deemed to be descriptive of the complete structure of a representative number of species of NM-F9 and NM-D4 able to express TF, MUC1 and glycophorin encompassed by the claims as one of skill in the art cannot envision all the subclones of NM-F9 and NM-D4 that could render the product subclones functional, e.g.,

in vitro induction of naive cytotoxic T cells against MUC1 and AGPA expressed in functional mature dendritic cells, said dendritic cells loaded with NM-F9 (Accession number DSM ACC2606) lysates in a prime reaction or *in vivo* induction of an IgG and IgM antibody responses in NOD/SCID mice reconstituted with human PBMC that were vaccinated with NM-F9 Accession number DSM ACC2606) cell lysates, indicating induction of T helper immune responses and memory immune responses against MUC1, TF and AGPA (p. 55, lines 24-30). Thus, the rejected claim encompasses an enormous genus of subclones of NM-F9 (Accession number DSM ACC2606) and NM-D4 (accession number DSM ACC2605) which require to express surface markers TF, MUC1 and glycophorin (GFP) that must meet very specific functional limitations.

Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., expression of potent antigens Tn, TA-MUC1, MUC1 and LeX), specific features and functional attributes (e.g., *in vitro* validation of induction of naive cytotoxic T cells against MUC1 and AGPA expressed in functional mature dendritic cells) that would distinguish different members of the claimed genus. In the instant case, no other characteristic in addition to the functional discussed above are disclosed. Such functional characteristics, however, do not allow one of skill in the art to distinguish the different members of the genera form each other. The examples in the specification do not disclose how a lysate of a subclone of NM-F9 or NM-D4 that have similar expression and density to cells surface markers in NM-F9 (Accession number DSM ACC2606) or NM-D4 (accession number DSM ACC2605) is able to induce a activation of naïve CTL against MUC1 and AGPA. As the *in vitro* activation of naive cytotoxic T cells against MUC1 and AGPA expressed in functional mature dendritic cells depends high density and stable expression of TF in NM-F9, for example, lysates from subclones that do not express high density of the TF antigen may not retain full or even partial activation of naïve CTL against MUC1 and AGPA, which are the carrier proteins for TF. There are not examples disclosed in the specification meeting the claimed limitations of rejected claim 3 subpart (c) with regard to structure and function other than for the NM-F9 (Accession number DSM ACC2606) and NM-D4 (accession number DSM ACC2605), which examples are only representative of two subclones of (a) or (b) within the broad genus of subclones expressing TF, MUC1 and glycophorin on the cell surface. Hence, the scope of the invention as embraced by the claims is not commensurate with the disclosure of the as filed specification for as there is not is no

structure/function relationship taught for the uncharacterized subclones of NM-F9 (Accession number DSM ACC2606) or NM-D4 (accession number DSM ACC2605) expressing TF, MUC1 and glycophorin on the cell surface.

Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 23 are rejected under 35 USC 103 as being unpatentable over Ichiyama M (2000, Kari Igaku Kenkyusho Zasshi, JP vol. 51, no. 3-4, pages 93-110, of record) in view of Benoist et al., (Immunology Letters 1992, pp. 45-55) and Karsten et al., (1998, Cancer Research

pp. 2541-2549, of record) and further in view of Springer G (1997, J Mol Med, pp. 594-602, of record.). **This is a new rejection necessitated by amendment of the claims in the response filed on 04-27-2009.**

Ichiyama M, discloses the cell line K562 contransfected with tumor-associated epithelial human mucin MUC1cDNA and with human B7cDNA (Figures 1-12).

Ichiyama M, do not specifically teach expression of glycophorin in K562.

However, at the time the invention was made, Benoist teaches that the K562 tumor cells present glycophorin A (GPA) on the cell surface. Indeed, Benoist discloses that increase of GPA expression on the cell surface may correlate with the resistance of K562 to NK cells (Abstract) . Benoist does not teach that enzymatic removal of the sialic acid covering the T antigen disaccharide in glycophorin to obtain asialoglycophorin enhances the immune effect of GPA.

However, at the time the invention was made, Springer teaches that crude preparations of enzymatically desialylated glycophorin from O RBC carrying high densities of TF in a pharmaceutical vaccine elicited specific TF-specific DTR responses reflecting activation of specific T cell.

The combined disclosure of Ichiyama, Benoist and Springer fail to teach MUC1 –TF positive K562.

However, at the time the invention was made, Karsten discloses the presence of the TF antigen (Galβ1-3GalNAcα-O-Ser/Thr (Core 1)) in the tandem repeat comprising the DTR motif (see for example, page 2545, col. 2; p. 2549, col. 1)

Therefore, in view of the benefits of a cancer vaccine cell line K562 that expresses MUC1/B7 after transfection with a vector encoding the full length molecules as taught by

Ichiyama M, said cell line further comprising on the cell surface TF as part of the DTR motif as taught by Karsten and glycophorin as disclosed by Benoist, it would have been *prima facie* obvious for one of ordinary skill in the art, to enzymatically remove the sialic acid covering the T antigen disaccharide in glycophorin to obtain asialoglycophorin in the cell line K562 that expresses MUC1 and glycophorin in an attempt to improve the efficacy of the vaccine formulation, as a person of ordinary skill in the art has good reason to pursue options within his grasp. The manipulation of previously identified DNA fragments and cell transformation systems is within the ordinary level of skill in the art of molecular biology. In turn, because the K562 that expresses MUC1/B7, TF and asialoglycophorin has the properties predicted in the prior art, e.g, specific activation of T cell responses, it would have been obvious to make the cell lines comprising MUC1, TF and asialoglycophorin on their surface.

Conclusion

Claims 1, 3, 5, 6, 11-12, 20, 22-24 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Maria Leavitt/

Maria Leavitt, PhD
Examiner, Art Unit 1633